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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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08/08/2006

Warren J. Leonard

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EXAMINER

LEAVITT, MARIA GOMEZ

ART UNIT

PAPER NUMBER

1633

NOTIFICATION DATE

DELIVERY MODE

01/04/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 10/579,988	<b>Applicant(s)</b> LEONARD ET AL.	
	<b>Examiner</b> MARIA LEAVITT	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08-12-2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 5,8,10-12,18,20 and 32-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 5,8,10-12,18,20 and 32-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08-12-2009</u> .  | 6) <input type="checkbox"/> Other: _____                          |

***Detailed Action***

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Status of claims. Applicants' response of 07-31-2009 has been entered. Claims 5, 8, 10-12, 18, 20 and 32-35 are pending. Claims 5, 18 and 32-35 has been amended by Applicants' amendment filed on 08-12-2009. Applicant's election of species: "a viral antigen" from the antigens recited in claim 11 was previously acknowledged. Applicant timely traversed the restriction (election) requirement in the reply filed on 05/02/2007.
3. Therefore, claims 5, 8, 10-12, 18, 20 and 32-35 are currently under examination to which the following grounds of rejection are applicable.

***Response to arguments***

***Withdrawn objection/ rejection in response to applicants' amendments***

***Claim objection***

In view of Applicants' arguments, objection to claims 32-35 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim has been withdrawn.

***Claim Rejections - 35 USC § 112- Second Paragraph***

In view of Applicants' amendment of claims 32 and 34 to change their dependency from claim 5, rejection of claims 32 and 34 under 35 U.S.C. 112, second paragraph, has been withdrawn.

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***Claim Rejections - 35 USC § 112 – First paragraph-written description***

In view of Applicants' remarks, in light of the guidance provided in the specification and knowledge available to one of ordinary skill in the art at the time of filing the present application and further in view of reconsideration of search under different premises, rejection of claims 5, 8, 10-12, 18, 20 and 32-35 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, has been withdrawn.

In view of the withdrawn rejection, applicants' arguments are rendered moot.

***Claim Rejections - 35 USC § 112 – First paragraph-enablement***

In view of Applicants' remarks, in light of the guidance provided in the specification and knowledge available to one of ordinary skill in the art at the time of filing the present application and further in view of reconsideration of search under different premises, rejection of claims 5, 8, 10-12, 18, 20 and 32-35 under 35 U.S.C. 112, first paragraph, first paragraph, as failing to comply with the enablement requirement, has been withdrawn.

In view of the withdrawn rejection, applicants' arguments are rendered moot.

***New grounds of rejection***

***Claim Rejections - 35 USC § 112- Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 5, 8, 10-12, 18, 20 and 32-35 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 18 have been amended to recite, “wherein the composition induces differentiation of at least one of the mature B cell”. As claims 5 and 18 encompass two compositions, namely, a composition comprising (i) or (iii), and a composition comprising an antigen, it is unclear which composition constitutes the proper antecedent bases for the induction of differentiation of at least one of the mature B cell. Thus the metes and bounds are not clearly set forth.

Claims 8, 10-12, 32 and 34 are indefinite insofar as they depend from claim 5. Claims 20, 33 and 35 are indefinite insofar as they depend from claim 18.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim(s) 5, 8, 10-12, 18, 20 and 32-35 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Newell et al. (US Publication No. 2003/0138433, Publication Date July 3, 2003; hereafter referred to as “Newell”), in view of Novak et al (US Publication No. .

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2003/0125524, of record; Publication date September 26, 2002; see SCORE search results for 10579988 and Search Result 20091207\_124249\_us-10-579-988a-1.rag.Results 3).

Newell discloses methods for promoting antigen-specific immune responses (page 1, paragraph [0003]) comprising obtaining B cells that have been originally isolated from a subject and subsequently contacted *in vitro* with a target antigen-conjugate to produce target antigen manipulated B cells. Moreover, Newell teaches that, “Primary encounter with antigens stimulates specific B cells not only to differentiate into cells that produce antibody at a high rate (plasma cells), but also to give rise to populations of memory cells”. Moreover, Newell states that these B cells have many characteristics that differ from naive B cells, (e.g., cells that have not encountered antigen)(page 1, paragraph [0010]). **(Current claims 5 and 18 steps a) and b), in part)**. Furthermore, *in vitro* contacting of the isolated B cells with a cytokine includes IL-4, IL-5, IL-6, IL-9, IL-10, and/or IL-13 (page 2, paragraph [0015])(**Current claims 5 and 18, step b) in part**). IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13 are primarily involved in providing optimal help for humoral immune responses such as IgE and IgG4 antibody isotype switching (page 2, paragraph [0009]). Moreover, Newell discloses that *ex vivo*-primed B cells, isolated from a subject are cultured, manipulated *in vitro*, and returned to the subject, including human subjects (page paragraph [0020]). Additionally, Newell teaches that an isolated B cell is a mature B cell within a lymphocyte population that is enriched for mature B cells by selectively eliminating T cells and other lymphocytes present in the PBMC sample, although a small number of T cells and other lymphocytes may be present (page 27;paragraph [0027]). **(Current claims 5 and 19, step c) and d); Claims 8 and 20)**. A list of antigens is disclosed, for example, in paragraphs [0017], [0018] [0071], including intracellular pathogens, bacterial antigens, proteins encoded by

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mutated oncogenes; viral proteins associated with tumors and others (**Current claims 10 and 11**). B cells are isolated from peripheral blood or from an *in vitro* hematopoietic progenitor cell culture (page 1, paragraph [0010], Claim 4)(**Current claim 12**).

Newell does not teach contacting the population of mature B cells or B progenitor cells with IL-21.

However, at the time the invention was made, Novak et al et al., discloses an isolated human cytokine of 162 amino acids in length, designated zalpha11 ligand, having 100% identity to the IL-21 polypeptide of SEQ ID NO: 1 of the claimed invention, (see, Score search result 3 for sequence alignment). Moreover, Novak et al., discloses that zalpha11 cytokine stimulates immune responses against B cell tumour, a virus, a parasite or a bacterium (page 18 [0125]). Moreover, zalpha11 ligand has an effect on the growth/expansion and/or differentiated state of B cells *in vivo* (page 18, [(0125)]). Zalpha11 Ligand also co-stimulates mature B cells stimulated with anti-CD40 antibodies (page 22, paragraph [0160]). Compounds identified as zalpha11 ligand agonists are also useful for expansion, proliferation, activation, differentiation, and/or induction or inhibition of specialized cell functions of cells involved in homeostasis of hematopoiesis and immune function (page 18, paragraph [0129]; page 22, paragraph [01610]) . Additionally, the zalpha11 cytokine receptor has the structure of a class I cytokine receptor which is shared by the class I cytokine receptor family of IL3, IL-5, IL-13, IL-15 (page 3, paragraph [0038]; page 22, paragraph 0154)] (**Current claims 5 and 19, step b) in part; claims 32-35**).

Both Newell and Novak disclose methods for stimulating proliferative responses of mature B cells with various cytokines. Novak teaches for IL-21 and its affect on B-cells and

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Newell provides the general methods for using B-cells for therapy. Therefore, in view of the benefits of an *ex vivo* method of inducing an immune response as taught by Newell et al., comprising the steps of contacting an isolated cell population comprising one or more mature B cell and a progenitor cell from a subject with a cytokine and an antigen, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made in an attempt to potentiate the immune response to the antigen and to enhance the therapeutic benefit to the host, to replace any of the IL-4, IL-5, IL-6, IL-9, IL-10, and/or IL-13 taught by Newell with a IL-21 disclosed by Novak to achieve the predictable result of inducing an immune response in a subject, particularly, because Novak et al. discloses that IL-21 is involved in the activation and proliferation of mature B cells in response to activating stimuli.

***Other art for comment***

The following art are cited to complete the record:

Ettinger R, et al, *J Immunol.* 2005 Dec 15;175(12):7867-79.

***Conclusion***

Claims 5, 8, 10-12, 18, 20 and 32-35 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



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To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maria Leavitt/

Maria Leavitt  
Primary Examiner, Art Unit 1633